PPTA
Plasma Protein Therapeutics Association

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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

VIA E-Mail & USPS

SUBJECT: From Concept to Consumer: Center for Biologics Evaluation and Research Working with Stakeholders on Scientific Opportunities for Facilitating Development of Vaccines, Blood and Blood Products, and Cellular, Tissue, and Gene Therapies; Public Workshop; Reopening of the Comment Period
Docket No. 2004N-0366

Dear Sir or Madam:

The Plasma Protein Therapeutics Association (PPTA) is pleased to provide these comments on the Food and Drug Administration's (FDA) public workshop, "From Concept to Consumer: Center for Biologics Evaluation and Research Working with Stakeholders on Scientific Opportunities for Facilitating Development of Vaccines, Blood and Blood Products, and Cellular, Tissue and Gene Therapies," [hereinafter "Workshop"]. PPTA is the international trade association and standards-setting organization for the world's major producers of plasma-derived and recombinant analog therapies. Our members provide 60 percent of the world's needs for Source Plasma and protein therapies. These include clotting therapies for individuals with bleeding disorders, immunoglobulins to treat a complex of diseases in persons with immune deficiencies, therapies for individuals who have alpha-1 anti-trypsin deficiency which typically manifests as adult onset emphysema and substantially limits life expectancy, and albumin which is used in emergency room settings to treat individuals with shock, trauma, burns, and other conditions. PPTA members are committed to assuring the safety and availability of these medically needed life-sustaining therapies.

We appreciate both the opportunity to participate in the Workshop and the ability to comment on the Workshop and the overall Critical Path Initiative. Over the course of the two years since FDA published the Whitepaper, "Innovation/Stagnation: Challenge and Opportunity on the Critical Path to New Medical Products" [hereinafter "Whitepaper"], and since holding the Workshop in 2004, PPTA has observed FDA targeting activities that advance the goals of the Critical Path Initiative. Some of these activities include the recent publication of a direct final rule that exempts Phase I clinical trials from current Good Manufacturing Practices (cGMP) regulations designed for marketed drug products and the Center for Biologics Evaluation and Research (CBER) workshop planned to re-examine behavioral risk donor deferrals in the era of nucleic acid testing (NAT). PPTA is encouraged by these efforts but worries that the efforts may not continue at an acceptable pace without proper funding, which includes a budget specifically targeted towards advancing the Critical

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Path Initiative. For any such far-reaching project to be successful, it needs to be appropriately funded and managed with goals and milestones developed to track progress.

With respect to the Workshop, PPTA wishes to reiterate the concerns expressed by our representative's presentation. In the presentation recommendations were made in three areas, each of which offers CBER the opportunity to assist in the development process of protein therapies. These areas are:

1. Clinical Trial Requirements

PPTA recommends that a fundamental review of clinical trial requirements occur, which will encourage development of therapies. Additionally as in all areas of regulation, global harmonization of requirements should be a goal. It is our view that requirements be less burdensome in order to facilitate access to therapies, while still protecting the health and safety of patients. At times, the mutual desires to develop new therapies, add indications to existing therapies, and make process improvements have been severely impacted by onerous requirements from CBER. The consequences of these requirements have stifled innovation and the ability to offer new therapies to patients. Some specific examples that were noted at the Workshop include:

- Requirement for placebo controls in evaluating indications for which overwhelming medical opinion exists that the therapy is efficacious. This requirement has made it impossible to include some indications in approved labeling; and
- Requirements for extensive clinical evaluation to support process changes, including powered studies to rejustify existing indications. An alternative approach that utilizes existing data, analytical comparability studies and, where appropriate, established preclinical models could significantly shorten development timelines and facilitate investments into important improvements to existing therapies.

As referenced in the Whitepaper, strengthening and rebuilding the disciplines of pharmacology and physiology is necessary to provide a bridge from animal to human studies and justify biomarkers as surrogates for more traditional clinical endpoints. PPTA supports and encourages such efforts as an adjunct to a more facile clinical development process.

2. Manufacturing Requirements

PPTA recognizes the challenge presented in manufacturing biological therapies. These therapies are often defined by the process of manufacturing rather than by composition alone. While recognizing the unique nature of biologics, PPTA believes opportunities exist to assist development, especially with regard to manufacturing scale up and changes. More often than not, CBER requires extensive clinical studies to support production scale up and process improvements. These requirements discourage, rather than encourage, increased production and process improvements. PPTA encourages CBER to utilize comparability assessments, preclinical evaluations, and if necessary bridging clinical studies in lieu of a

second almost duplicative study of the initial clinical program. This would facilitate the entire process and encourage improvements to existing facilities and processes.

3. Pathogen Safety Requirements

Great strides have been made in the area of pathogen safety. It is important that CBER, industry, and stakeholders work together to communicate risks and technological advancements in the face of emerging infectious diseases and existing pathogens. While taking this into consideration coupled with the goal of global harmonization, PPTA sponsors the Emerging Infectious Diseases (EID) Roundtable. Two EID Roundtables have been held. PPTA encourages CBER to remain an active participant in this initiative.

It is also important to review existing test requirements and donor deferral and lookback policies in light of new information, improved testing of donors and manufacturing pools, and inclusion of robust pathogen clearance processes in manufacturing. Resources currently devoted to donor deferral management and inefficient and unnecessary lookback procedures could be better invested in therapy innovations.

PPTA appreciates the opportunity to comment on the Critical Path Workshop and overall the Critical Path Initiative. We are enclosing a copy of our letter FDAA04015, dated July 30, 2004, which provided comments on the Whitepaper. Those comments are still relevant today. Should you have any questions regarding these comments or would like additional information, please contact PPTA. Thank you for your consideration, and we look forward to working on the exciting possibilities included in the Critical Path Initiative.

Respectfully submitted,

Mary Gustafson
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Enclosure